

Brief note

Vesicle formation of 1:1 cationic and anionic surfactant mixtures in *N,N*-dimethylformamide and tetrahydrofuran solutions

J.-B. Huang *, R. Yang, B.-Y. Zhu, X. He, H.L. Fu

Institute of Physical Chemistry, Peking University, Beijing 100871, PR China

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1. Introduction

In the last two decades, many works on vesicle formation from natural amphiphiles (mainly phospholipids) and synthetic surfactants were reported [1,2]. However, up to 10 years ago amphiphiles used to form vesicles are mainly the double chained compounds including natural and synthesized amphiphiles. In 1989, Kaler et al. [3] revealed the vesicle formation from mixed cationic and anionic surfactants using cetyltrimethyl-ammonium tosylate and sodium dodecylbenzene sulfonate. Similar work was done in our laboratory, using mixed surfactants of carboxylate and alkyltrimethylammonium compounds [4,5]. However, most works on vesicle formation have been involved in aqueous systems and those in non aqueous systems are less. Some works about vesicle formation in aprotic solvent systems were reported [6,7], which were concen-

trated on the systems of double-chained fluorocarbon surfactants [8–11]. On the other hand, the studies about vesicle formation in non aqueous polar solvent and mixed polar solvents' systems are mainly on the liposome of phospholipids [12–14]. Comparing with phospholipids and other double-chained amphiphiles, the cationic and anionic surfactants used as precursors for vesicle formation have the predominances of simple structure, excellent stability, and convenience in production. Therefore, investigation on vesicle formation by cationic and anionic surfactants is of great significance in both theoretics and applications. It is well known that many drugs are insoluble in water but soluble in organic solvents, and many useful reactions can be carried out in nonaqueous systems. However, the investigations about vesicle formation of mixed cationic and anionic surfactants in non-aqueous polar solvents are scanty. Obviously, it is important to study the vesicle formation in non aqueous or mixed solvents. In a previous paper [15], we reported the

* Corresponding author.

vesicle formation of 1:1 cationic and anionic surfactant mixtures in pure ethanol, which is different from the early studies showing that ethanol addition deteriorates the molecular order in lipid bilayers [16–20]. An explanation based on the effect of medium dielectric constant was suggested [15]. Recently, spontaneous vesicle formation of 1:1 cationic and anionic was also observed in iso-propanol and 1-propanol [21]. In this work, we develop the investigation of vesicle formation in tetrahydrofuran (THF), and *N,N*-dimethylformamide (DMF), which are important solvents for many organic chemicals. Different kind of vesicle including multilamellar vesicle and multi-layer structures were observed in these systems. These

results not only support the explanation based on the effect of medium dielectric constant [15] very well, but provide a new way to control the chemical reaction in these widely used solvents.

2. Experimental

2.1. Materials

Sodium alkylcarboxylates ($C_n\text{COONa}$, $n = 9, 11$) were prepared by neutralizing the corresponding carboxylic acid ($C_n\text{COOH}$) with NaOH in ethanol, then the solvent was removed and $C_n\text{COONa}$ was vacuum dried. $C_9\text{COOH}$ was double

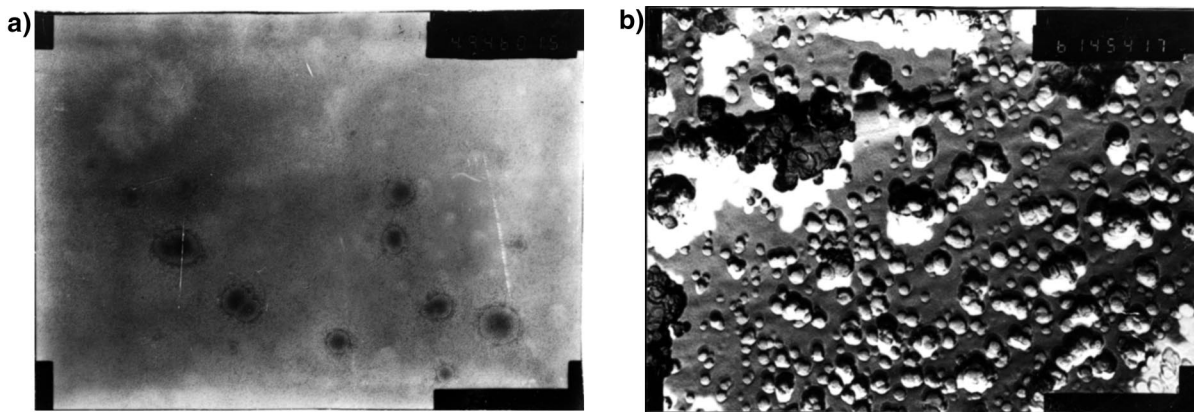


Fig. 1. Electron image in pure DMF of 1:1 $C_9\text{COONa-C}_{10}\text{NMBr}$ ($c = 1.5 \times 10^{-2} \text{ mol dm}^{-3}$) systems, with sonication, observed by (a) negative-staining technique, and (b) freeze fracture technique.

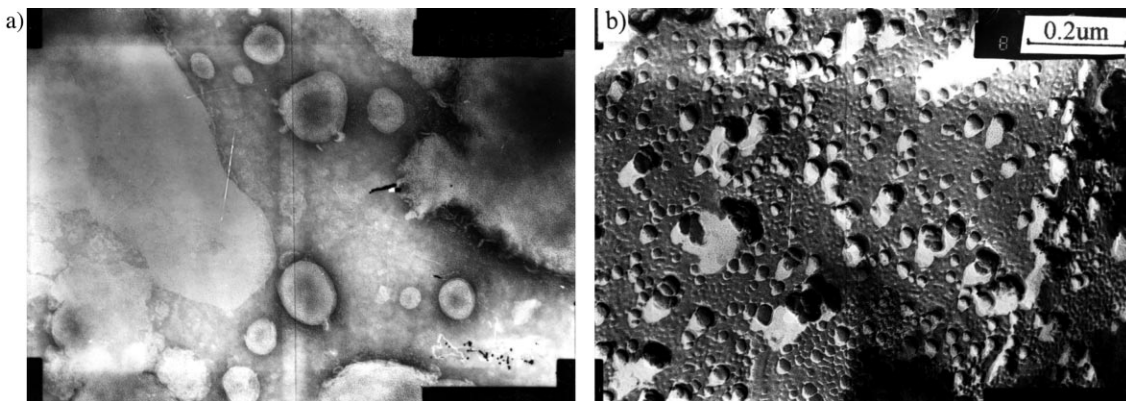


Fig. 2. Electron microscopic image in pure DMF of 1:1 $C_{11}\text{COONa-C}_8\text{NMBr}$ ($c = 1.30 \times 10^{-2} \text{ mol dm}^{-3}$) systems, without sonication, observed by (a) negative-staining technique, and (b) freeze fracture technique.

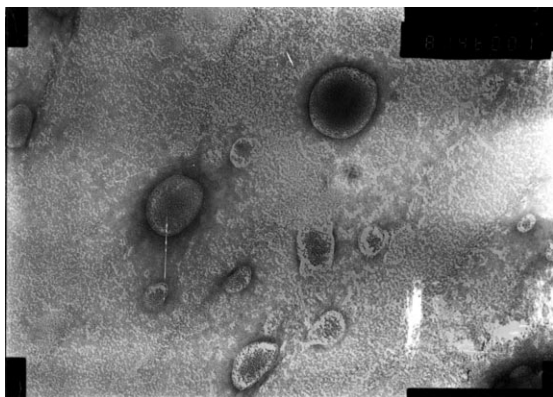


Fig. 3. Electron microscopic image in 1:1 $C_{11}COONa-C_{12}NMBr$ DMF system observed by negative staining technique ($c = 8.0 \times 10^{-3} \text{ mol dm}^{-3}$), enlarging 81 000 times.

distilled and $C_{11}COOH$, recrystallized five times from an ethanol–water mixed solvent (m.p. 43–44°C). Alkyltrimethyl ammonium bromides (C_mNMBr $m = 8, 10, 12$) were synthesized from n -alkyl bromide and tri-methyl amine. The products were recrystallized five times from an ethanol–acetone mixture [4]. The purities of all the surfactants were examined by measuring the surface tensions of aqueous solutions using drop volume method [22] and no surface tension minimum was found in their surface tension curves ($\gamma - \log C$). THF was purified as following procedure: (1) washed with $FeSO_4/H_2SO_4$ solution to remove the trace of peroxide; (2) dried > 24 h by $CaCl_2$; (3)

refluxed with lithium aluminum hydride 4–5 h then distilled. DMF was firstly dried > 24 h by anhydrous $MgSO_4$ and KOH , distilled. Deionized water was treated with $KMnO_4$ and distilled before use. Other reagents were products of Beijing Chemical Co., A.R. Grade.

2.2. Methods

The mixed surfactant vesicles were prepared by simply 1:1 (molar ratio) mixing the cationic and anionic surfactant in the solvent selected at room temperature ($\approx 30^\circ C$) or by sonicating the mixed surfactant solution for 0.5 h at $50^\circ C$ (Sonicator: Haitung CQ-250). Micrographs were obtained with an electron microscope (JEM-100CXII) using the freeze-fracture technique or negative-staining technique for sample preparation. A post-staining method was adopted in the sample preparation of negative staining technique: a few drops of the sample solution were applied to carbon-coated Cu grids and dried, then a drop of uranyl acetate ethanol solution was added as the staining agent. The staining process would be 1–2 min depending on different solvents. The phase transition temperature T_c of the vesicle in 1:1 mixed cationic and anionic surfactant system was measured by use of differential scanning calorimeter (Dupont 1090; with the heating rate of $1.5^\circ C \text{ min}^{-1}$). The endothermic peak top was determined as the T_c value of the system.

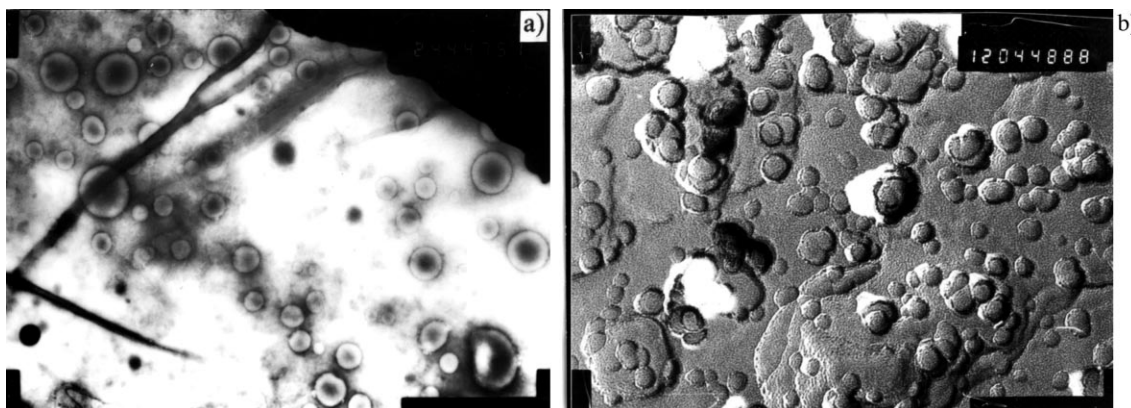


Fig. 4. Electron microscopic image in 90% THF (volume ratio) of 1:1 $C_{11}COONa-C_8NMBr$ ($c = 2.5 \times 10^{-2} \text{ mol dm}^{-3}$) systems, without sonication, observed by (a) negative-staining technique, and (b) freeze fracture technique.

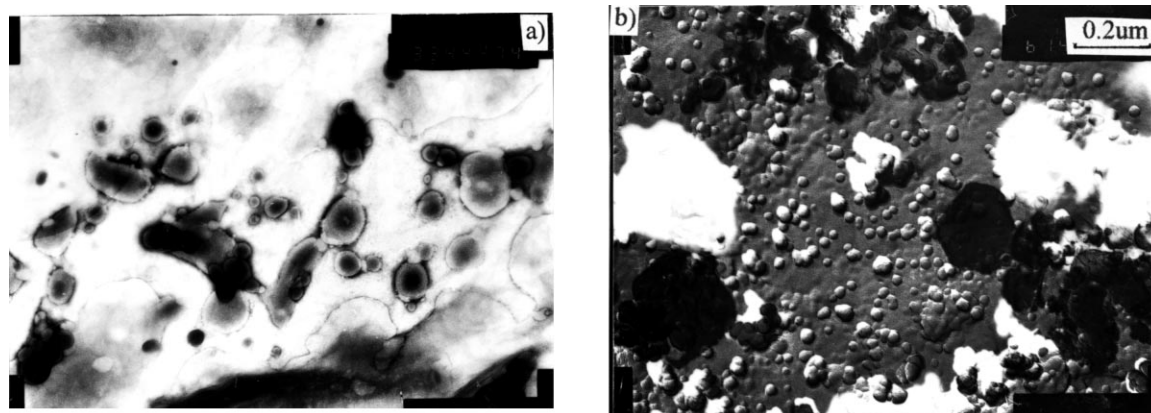


Fig. 5. Electron microscopic image in of 1:1 $C_9COONa-C_{10}NMBr$ (98%THF, $c = 2.0 \times 10^{-2} \text{ mol dm}^{-3}$) system, observed by (a) negative-staining technique, and (b) freeze fracture technique.

Table 1
Vesicle formation in THF–water solution of mixed surfactant systems^a

| 1:1 Mixed systems | Concentration $c/\text{mol}^{-1} \text{ dm}^{-3}$ | $V_{\text{THF}} = 0$ | | $V_{\text{THF}} = 0.5$ | | $V_{\text{THF}} = 0.75$ | | $V_{\text{THF}}^b = 0.95$ | |
|--------------------------|---|----------------------|----|------------------------|----|-------------------------|----|---------------------------|----|
| | | N.S. | S. | N.S. | S. | N.S. | S. | N.S. | S. |
| $C_9COONa-C_{10}NMBr$ | 2.0×10^{-2} | – | + | + | + | + | + | + | + |
| $C_{11}COONa-C_8NMBr$ | 2.5×10^{-2} | + | + | + | + | + | + | + | + |
| $C_{11}COONa-C_{12}NMBr$ | 7.5×10^{-3} | + | + | + | + | + | + | + | + |

^a S. = sonication; N.S. = without sonication; + = vesicle formed; – = no vesicle.

^b V_{THF} , denote the ratio of THF volume and total volume.

Table 2
Vesicle formation in DMF–water solution of mixed surfactant systems^a

| 1:1 Mixed systems | Concentration $c/\text{mol} \text{ dm}^{-3}$ | $V_{\text{DMF}}^b = 0.3$ | | $V_{\text{DMF}} = 0.5$ | | $V_{\text{DMF}} = 0.75$ | | $V_{\text{DMF}} = 1.0$ | |
|--------------------------|--|--------------------------|----|------------------------|----|-------------------------|----|------------------------|----|
| | | N.S. | S. | N.S. | S. | N.S. | S. | N.S. | S. |
| $C_9COONa-C_{10}NMBr$ | 1.5×10^{-2} | + | + | + | + | + | + | + | + |
| $C_{11}COONa-C_8NMBr$ | 1.3×10^{-2} | | | + | + | + | + | + | + |
| $C_{11}COONa-C_{12}NMBr$ | 8.0×10^{-3} | + | + | + | + | | | + | + |

^a S. = sonication; N.S. = without sonication; + = vesicle formed; – = no vesicle.

^b V_{DMF} , denote the ratio of THF volume and total volume.

3. Results and discussion

Solutions of three pairs of cationic and anionic surfactants (1:1 $C_9COONa-C_{10}NMBr$, $C_{11}COONa-C_{12}NMBr$ and $C_{11}COONa-C_8NMBr$) in DMF, THF, and the aqueous mixtures of each were studied. At room temperature ($\approx 30^\circ\text{C}$), it is

difficult to solve the mixed surfactants in pure THF. However, tiny amount of water addition can make the system clear. For example, $C_{11}COONa-C_{12}NMBr$ in 96% THF + 4% H_2O and $C_9COONa-C_{10}NMBr$ in 98% THF + 2% H_2O systems are clear. The DMF solutions studied are opalescent no matter for pure DMF or their

aqueous mixed systems. The systems were investigated by electron microscopy (EM) and differential scanning calorimeter (DSC). The EM results have been shown in Figs. 1–5, and Tables 1 and 2. It is seen that the 1:1 cationic–anionic surfactant vesicles formed in DMF, in nearly pure THF and in the aqueous mixtures of each. Particularly the EM images by negative staining technique indicate the globular aggregates are typical vesicles, composed of enclosed surfactant membrane with uranyl acetate solution inner and outer. The sizes of vesicles are $\approx 15\text{--}35$ nm determined from the EM images obtained by the freeze-fracture technique. The DSC curves were shown in Fig. 6, which further confirmed the vesicle formation of 1:1 mixed cationic and anionic surfactant in THF systems. Some results of phase transition temperature (T_c) were listed in Table 3.

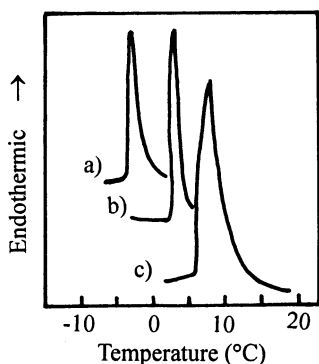


Fig. 6. DSC curves in (a) 1:1 $C_{11}\text{COONa-C}_8\text{NMBr}$ (96% THF, $c = 2.5 \times 10^{-2}$ mol dm^{-3}) system; (b) 1:1 $C_{11}\text{COONa-C}_{12}\text{NMBr}$ (98% THF, $c = 7.5 \times 10^{-3}$ mol dm^{-3}) system, (c) 1:1 $C_9\text{COONa-C}_{10}\text{NMBr}$ (90% THF, $c = 2.0 \times 10^{-2}$ mol dm^{-3}) system.

Table 3
 T_c of cationic–anionic surfactant mixtures in THF

| 1:1 Mixed systems | $c/\text{mol}\cdot\text{dm}^{-3}$ | Solvents | T_c (°C) |
|--|-----------------------------------|----------|------------|
| $C_9\text{COONa-C}_{10}\text{NMBr}$ | 2.0×10^{-2} | 98% THF | 7.5 |
| $C_{11}\text{COONa-C}_{12}\text{NMBr}$ | 7.5×10^{-2} | 96% THF | 4.0 |
| $C_{11}\text{COONa-C}_8\text{NMBr}$ | 2.5×10^{-2} | 90% THF | –2.0 |

It is seen that the three pairs of cationic–anionic surfactants investigated can form vesicles in pure DMF and all the mixed aqueous solvents of various composition investigated, with or without sonication. After carefully studying the EM images of catanionic surfactant vesicles formed in DMF and THF systems, it is also interesting to note that the vesicles formed in these systems are multilamellar vesicles (more obviously shown in Figs. 3 and 4, and Fig. 7). In the magnified EM images (Fig. 7) the distance between two layers of vesicle can be measured to be 3–4 nm from them. The multilayer structures were also observed in Fig. 7c.

The 1:1 cationic and anionic surfactant vesicles formed in these systems are also quite stable. By EM observation it was found that in $C_{11}\text{COONa-C}_{12}\text{NMBr-DMF}$, $C_9\text{COONa-C}_{10}\text{NMBr-DMF}$, $C_{11}\text{COONa-C}_{12}\text{NMBr-96\% THF}$ and $C_9\text{COONa-C}_{10}\text{NMBr-98\% THF}$ systems vesicles can be stable after 6 weeks aging (Fig. 8). Nevertheless, in these systems there was still vesicle existence after through a very large temperature variation — heated to 50°C (aging for 15 min) or cooled to –17°C (aging for an hour) then returned to $\approx 30^\circ\text{C}$ (Figs. 9 and 10). All these results demonstrate that the mixed cationic and anionic surfactants display superior vesicle-forming capability and stability in DMF and THF. It is worthy to note that for 1:1 $C_9\text{COONa-C}_{10}\text{NMBr}$ system no vesicles were found in water without sonication (Table 1), whereas vesicles form spontaneously in the DMF or nearly pure THF systems investigated (Tables 1 and 2). It is implied that the vesicle formability of cationic and anionic surfactants in medium containing DMF or THF is better than that in pure water.

In previous work [15], we suggested an explanation about vesicle formation in ethanol solutions based on medium dielectric effect. According to the Coulomb's law, the relative dielectric constant of medium will affect the electrostatic force between two ionic surfactants directly. Thus the ethanol addition to aqueous system will enlarge the electrostatic interaction between the cationic and anionic surfactants since the dielectric constant of ethanol is much lower than the water. This effect is of advantage in energy requirement

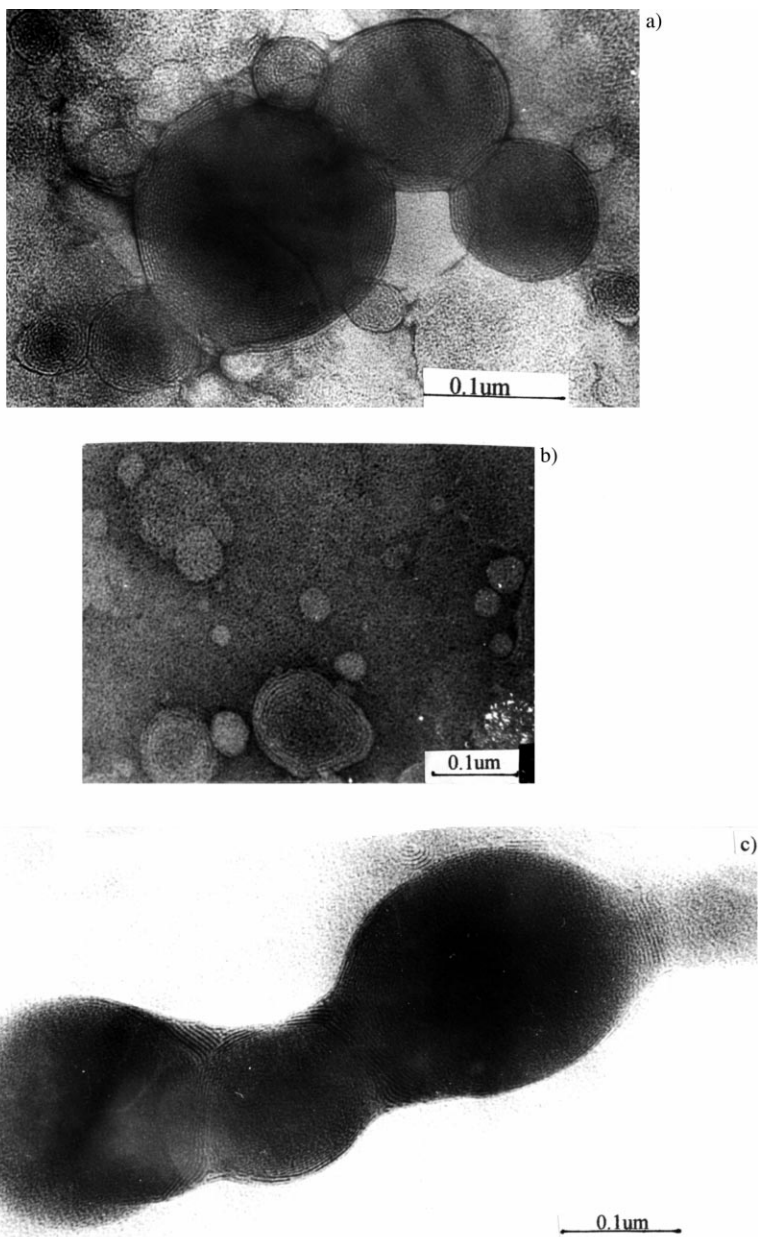


Fig. 7. Electron microscopic image in (a) 1:1 $C_{11}COONa-C_{12}NMBr$ (96% THF, $c = 7.5 \times 10^{-3} \text{ mol dm}^{-3}$) system; (b) 1:1 $C_9COONa-C_{10}NMBr$ (98% THF, $c = 2.0 \times 10^{-2} \text{ mol dm}^{-3}$) system; (c) 1:1 $C_{11}COONa-C_8NMBr$ (90% THF, $c = 2.5 \times 10^{-2} \text{ mol dm}^{-3}$) system.

and the molecular packing geometry [23] for vesicle formation. In suitable case, it may overcome the disadvantageous influence of ethanol addition on the hydrophobic effect [24] and resulting in a

more favorable energy and geometric conditions for vesicle formation.

According to this explanation, it can be predicted that vesicle formations of the cationic and

anionic surfactant in non-aqueous polar solvents with lower dielectric constant are possible. In fact this explanation was already supported by the work [21] recently published by us. The results in this work coincides with the prediction and support our previous explanation [15] strongly. The relative dielectric constants of DMF and THF (26.7 and 7.6, respectively) are lower than that of water (78.5) [25], and it is understandable that the

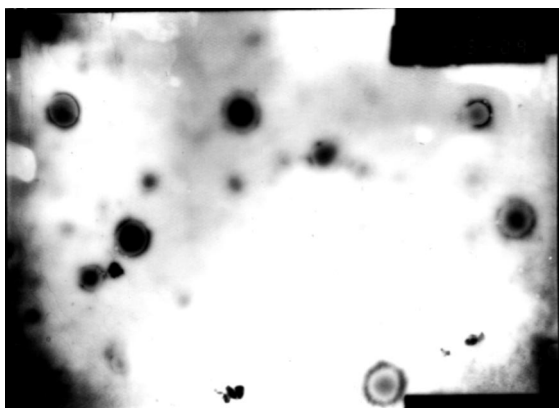


Fig. 8. Electron microscopic image in 1:1 $C_{11}COONa-C_{12}NMBR$ -DMF system observed by negative staining technique ($c = 8.0 \times 10^{-3} \text{ mol dm}^{-3}$), aging 6 weeks. Enlarged 12 000 times.

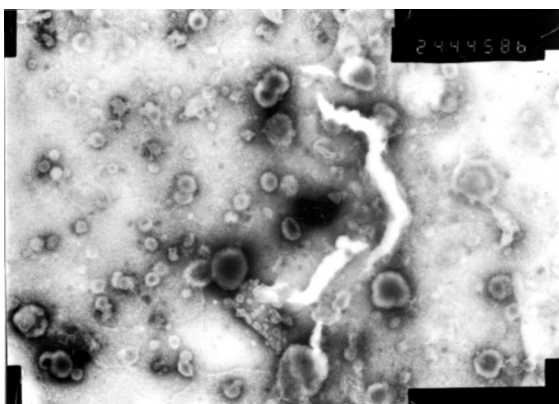


Fig. 9. Electron microscopic image in 1:1 $C_9COONa-C_{10}NMBR$ (98% THF, $c = 1.5 \times 10^{-2} \text{ mol dm}^{-3}$) systems, after $-17^\circ\text{C} \times 1 \text{ h}$ observed by negative staining technique at room temperature. Enlarged 24 000 times.

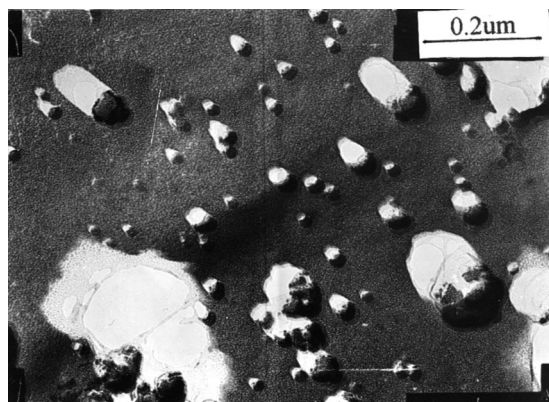


Fig. 10. Electron microscopic image in pure DMF of 1:1 $C_9COONa-C_{10}NMBR$ ($c = 2.0 \times 10^{-2} \text{ mol dm}^{-3}$) system, after $50^\circ\text{C} \times 15 \text{ min}$, observed by freeze fracture technique at room temperature.

cationic and anionic surfactant vesicles formed in these systems.

4. Conclusion

The vesicle formations of three pairs of 1:1 cationic-anionic surfactants in DMF, THF, and the aqueous mixtures of each were investigated. The cationic and anionic surfactants can form vesicles in the mixtures of DMF–water, THF–water and in pure DMF, spontaneously. And multilamellar vesicles were found in pure DMF and THF(with tiny amount of water) systems. All these results support the explanation previously suggested based on the medium dielectric effect very well. The outstanding vesicle-forming capability and stability of the simple cationic and anionic surfactant in DMF and THF may open a vast vista for enlarging the application scope of the functions of vesicular system beyond the limit of aqueous solution and water soluble material, since many important chemical reactions are carried out in these non-aqueous solvents.

Acknowledgements

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References

- [1] J.H. Fendler, *Membrane Mimetic Chemistry*, Wiley, New York, 1982 (Chapter 6).
- [2] T. Kunitake, in: K.L. Mittal, P. Bothorel (Eds.), *Surfactants in Solution*, vol. 5, Plenum, New York, 1986, p. 727 (in Russian).
- [3] E.W. Kaler, A.K. Murthy, B.E. Rodriguez, T.A.N. Zasadzinski, *Science* 245 (1989) 1371.
- [4] G.-X. Zhao, J.-B. Huang, *Acta. Phys. Chim. Sinica* 8 (1992) 583.
- [5] J.-B. Huang, G.-X. Zhao, *Colloids Polym. Sci.* 273 (1995) 156.
- [6] H. Kunieda, M. Akimaru, N. Ushio, et al., *J. Colloids Interface Sci.* 156 (1993) 446.
- [7] J.-M. Kim, T. Kunitake, *Chem. Lett.* 959.
- [8] Y. Isikawa, H. Kuwahara, T. Kunitake, *J. Am. Chem. Soc.* 111 (1989) 8530.
- [9] Y. Isikawa, H. Kuwahara, T. Kunitake, *J. Am. Chem. Soc.* 116 (1994) 5579.
- [10] H. Kuwahara, Y. Isikawa, T. Kunitake, *J. Am. Chem. Soc.* 115 (1993) 3002.
- [11] Y. Isikawa, H. Kuwahara, T. Kunitake, *Chem. Lett.* (1989) 1737.
- [12] T.J. McIntosh, A.D. Magid, S.A. Simon, *Biochemistry* 28 (1989) 7907.
- [13] R.V. McDaniel, T.J. McIntosh, S.A. Simon, *Biochim. Biophys. Acta* 731 (1983) 97.
- [14] N. Kimizuka, T. Wakiyama, T. Kunitake, et al., *J. Am. Chem. Soc.* 118 (1996) 5808.
- [15] J.-B. Huang, B.-Y. Zhu, G.-X. Zhao, et al., *Langmuir* 13 (1997) 5759.
- [16] C.D. Tran, P.L. Klahn, A. Romero, et al., *J. Am. Chem. Soc.* 100 (1978) 1622.
- [17] A.D. Dalton, K.W. Miller, *Biophys. J.* 65 (1993) 1620.
- [18] S.A. Simon, T.J. McIntosh, *Biochim. Biophys. Acta* 773 (1984) 169.
- [19] J. Zeng, K.E. Smith, P.L.-G. Chong, *Biophys. J.* 65 (1993) 1404.
- [20] S.J. Regan, B. Czech, A. Singh, *J. Am. Chem. Soc.* 103 (1982) 456.
- [21] J.B. Huang, B.Y. Zhu, M. Mao, et al., *Coll. Polym. Sci.* 277 (1999) 354.
- [22] B.-Y. Zhu, G.-X. Zhao, *HuaXueTongBao* 6 (1981) 341.
- [23] J.N. Israelachvili, *Intermolecular and Surface Forces*, Academic Press, London, 1985 (Chapter 16).
- [24] A. Ray, *Nature* 231 (1971) 314.
- [25] J.A. Dean, *Large's Handbook of Chemistry*, 13th ed., McGraw-Hill, 1985.